```
FILE 'REGISTRY' ENTERED AT 10:40:50 ON 21 NOV 2002

=> S HYDANTOINASE/CN
L1            1 HYDANTOINASE/CN

=> D

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9030-74-4  REGISTRY
CN   Dihydropyrimidinase (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   5,6-Dihydropyrimidine amidohydrolase
CN   Cyclic amide amidohydrolase
CN   Cyclic ureide imidase
CN   d-5-Phenylhydantoinase
CN   D-Hydantoin amidohydrolase
CN   D-Hydantoinase
CN   Dihydropyrimidine amidohydrolase
CN   DL-Hydantoinase
CN   E.C. 3.5.2.2
CN     ***Hydantoinase***
CN   Hydropyrimidine hydrase
CN   Imidase
CN   L-Hydantoinase
CN   Phenylhydantoinase
DR   172399-52-9
MF   Unspecified
CI   MAN
LC   STN Files:   AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
       CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, EMBASE,
       IFICDB, IFIPAT, IFIUDB, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             331 REFERENCES IN FILE CA (1962 TO DATE)
              11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             332 REFERENCES IN FILE CAPLUS (1962 TO DATE)


=> S CARBAMOYLASE/CN
L2            0 CARBAMOYLASE/CN

=> HYDANTOIN/CN
HYDANTOIN IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> S HYDANTOIN/CN
L3            1 HYDANTOIN/CN

=> D

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   461-72-3  REGISTRY
CN   2,4-Imidazolidinedione (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Imidazolin-4(or 5)-one, 2-hydroxy- (7CI)
CN     ***Hydantoin (6CI, 8CI)***
OTHER NAMES:
CN   Glycolylurea
CN   Imidazole-2,4(3H,5H)-dione
FS   3D CONCORD
DR   345341-10-8
MF   C3 H4 N2 O2
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, GMELIN*,
       HODOC*, IFICDB, IFIPAT, IFIUDB, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT,
       RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
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     Other Sources:   EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)


/ Structure 1 in file .gra /


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

            1211 REFERENCES IN FILE CA (1962 TO DATE)
             364 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1217 REFERENCES IN FILE CAPLUS (1962 TO DATE)
              22 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


=> S ALLYSINE/CN
L4            1 ALLYSINE/CN

=> D

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   1962-83-0  REGISTRY
CN   Norleucine, 6-oxo- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Norvaline, 5-formyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN   .alpha.-Aminoadipic .delta.-semialdehyde
CN   .alpha.-Aminoadipic acid .delta.-semialdehyde
CN   2-Amino-5-formylvaleric acid
CN   6-Oxo-DL-norleucine
CN     ***Allysine***
FS   3D CONCORD
DR   34897-38-6
MF   C6 H11 N O3
LC   STN Files:   ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS,
       EMBASE, MEDLINE, PROMT, TOXCENTER
         (*File contains numerically searchable property data)


/ Structure 2 in file .gra /


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              60 REFERENCES IN FILE CA (1962 TO DATE)
               1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
              60 REFERENCES IN FILE CAPLUS (1962 TO DATE)
              12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


FILE 'CAPLUS' ENTERED AT 10:43:42 ON 21 NOV 2002

=> S HYDANTOINASE OR L1
             274 HYDANTOINASE
              41 HYDANTOINASES
             279 HYDANTOINASE
                   (HYDANTOINASE OR HYDANTOINASES)
             333 L1
L5           389 HYDANTOINASE OR L1

=> S HYDANTOIN OR L3
            6332 HYDANTOIN
            2072 HYDANTOINS
            6980 HYDANTOIN
                   (HYDANTOIN OR HYDANTOINS)
            1217 L3
L6          7191 HYDANTOIN OR L3

=> S ALLYSINE OR L4
              70 ALLYSINE
               1 ALLYSINES
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            70 ALLYSINE
                 (ALLYSINE OR ALLYSINES)
            62 L4
L7         112 ALLYSINE OR L4

=> S L5 AND L6 AND L7
L8           1 L5 AND L6 AND L7

=> D CBIB ABS

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
2002:107576   Document No. 136:149991  Process for the preparation of
      ***allysine***   acetal.  Krimmer, Hans-Peter; May, Oliver; Klement, Ingo;
     Drauz, Karlheinz; Reichert, Dietmar (Degussa A.-G., Germany).  PCT Int.
     Appl. WO 2002010424 A1 20020207, 16 pp.  DESIGNATED STATES: W:  AU, BR,
     CA, CN, CZ, HR, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RU, SG, SI, SK,
     ZA; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
     PT, SE, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO 2001-EP7387
     20010628.  PRIORITY: DE 2000-10037115 20000728.
GI


/ Structure 3 in file .gra /


AB   The present invention relates to the prepn. of compds. of formula (I) from
     the corresponding   ***hydantoins***   (II) by means of an enzymic process
     where R represents C1-C8 alkyl, C2-C4 alkenyl, preferably ethylenyl,
     C6-C18 aryl, C7-C19 aralkyl, or C1-C8 acyl.  The   ***hydantoin***   , II
     is subjected to a reaction catalyzed   ***hydantoinase***   ,
       ***hydantoin***   racemase and a L- or D- specific carbamoylase.  The
     L-compd. is preferably formed.


=> S CARBAMOYLASE
            82 CARBAMOYLASE
            10 CARBAMOYLASES
L9          85 CARBAMOYLASE
                 (CARBAMOYLASE OR CARBAMOYLASES)

=> S L5 AND L6 AND L9
L10         39 L5 AND L6 AND L9

=> S L10 NOT L8
L11         38 L10 NOT L8

=> D 1-39 CBIB ABS

L11  ANSWER 1 OF 38  CAPLUS  COPYRIGHT 2002 ACS
2002:789426  Complete Conversion of D,L-5-Monosubstituted   ***Hydantoins***
     with a Low Velocity of Chemical Racemization into D-Amino Acids Using
     Whole Cells of Recombinant Escherichia coli.  Martinez-Rodriguez, Sergio;
     Las Heras-Vazquez, Francisco Javier; Clemente-Jimenez, Josefa Maria;
     Mingorance-Cazorla, Lydia; Rodriguez-Vico, Felipe (Departamento de
     Quimica-Fisica Bioquimica y Quimica Inorganica Edificio C.I.T.E. I,
     Universidad de Almeria, La Canada de San Urbano, E-04120, Spain).
     Biotechnology Progress ACS ASAP (English).  CODEN: BIPRET.  ISSN:
     8756-7938.  Publisher: American Chemical Society.
AB   A reaction system was developed for the prodn. of D-amino acids from
     D,L-5-monosubstituted   ***hydantoins***   with a very slow rate of
     spontaneous racemization.  For this purpose the D-  ***hydantoinase***
     and D-  ***carbamoylase***   from Agrobacterium radiobacter NRRL B11291
     were cloned in sep. plasmids and expressed in Escherichia coli.  The third
     enzyme,   ***hydantoin***   racemase, was cloned from Agrobacterium
     tumefaciens C58.  The   ***hydantoin***   racemase amino acid sequence was
     significantly similar to those previously described.  A reaction system
     consisting of recombinant Escherichia coli whole cell biocatalysts contg.
     sep. expressed D-  ***hydantoinase***   , D-  ***carbamoylase***   , and
       ***hydantoin***   recemase showed high substrate specificity and was
     effective toward both aliph. and arom. D,L-5-monosubstituted
       ***hydantoins***   .  After optimizing reaction conditions (pH 8 and 50
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:degree.C), 100% conversion of D,L-5-(2-methylthioethyl)- ***hydantoin*** (15 mM) into D-methionine was obtained in 30 min.

L11 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2002 ACS
2002:754602 Document No. 137:262002 Process for the production of enantiomer-enriched alpha-substituted carboxylic acids. May, Oliver; Syldatk, Christoph; Vielhauer, Oliver; Werner, Markus (Degussa Ag, Germany). PCT Int. Appl. WO 2002077250 A2 20021003, 22 pp. DESIGNATED STATES: W: CA, HR, IL, IN, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP2880 20020315. PRIORITY: DE 2001-10115000 20010326.
AB The present invention describes a process for the prodn. of enantiomer-enriched .alpha.-substituted carboxylic acids with the assistance of the ***hydantoinase*** / ***carbamoylase*** enzyme system. The compds. to be used comprise substances of the general formulas (I) or (II) in which X means 0, S, CH2. Thus, 2-benzyl-succinamic acid was enantioselectively deamidated by D-***carbamoylase*** .

L11 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2002 ACS
2002:754567 Document No. 137:275014 Purification, cloning, and characterization of D- ***carbamoylase*** from Arthrobacter crystallopoietes DSM 20117 and use of D- ***carbamoylase*** for preparation of D-amino acids from ***hydantoins*** . Drauz, Karlheinz; May, Oliver; Bommarius, Andreas; Syldatk, Christoph; Altenbuchner, Josef; Werner, Markus; Siemann-Herzberg, Martin (Degussa AG, Germany). PCT Int. Appl. WO 2002077212 A2 20021003, 49 pp. DESIGNATED STATES: W: BR, CA, CN, CZ, IL, IN, JP, KR, SG, ZA; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP1840 20020221. PRIORITY: DE 2001-10114999 20010326.
AB The present invention relates to a new D- ***carbamoylase*** and the gene sequences which code for this from the organism Arthrobacter crystallopoietes DSM 20117. Plasmids, vectors, microorganisms, particular primers and specific possible uses of the enzymes according to the invention are also mentioned. The invention moreover describes a new process for the discovery of enzymes which can be employed in a process for the prepn. of D-amino acids starting from 5'-substituted ***hydantoins*** .

L11 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2002 ACS
2002:595031 Document No. 137:139489 Process for the enzymatic preparation of enantiomer-enriched amino acids. Boesten, Wilhelmus Hubertus Joseph; Kierkels, Joannes Gerardus Theodorus (DSM N.V., Neth.). PCT Int. Appl. WO 2002061107 A2 20020808, 12 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-NL72 20020131. PRIORITY: NL 2001-1017250 20010131.
AB Process is provided for the prepn. of a chiral amino acid enriched in the D-enantiomer, in which a racemic mixt. of of the corresponding N-carbamoylamino acid is brought into contact with a D-***carbamoylase*** with ammonia being liberated, the ammonia being subsequently removed with the aid of a bivalent metal salt of a phosphate, a monohydrogen phosphate or a dihydrogen phosphate ion. In one embodiment the enzymic decarbamoylation is carried out in the presence of a bivalent metal salt of a phosphate ion, a monohydrogen phosphate ion or a dihydrogen phosphate ion. In another embodiment the reaction mixt. is brought into contact via an external loop, after sepn. of the solid present, with the bivalent metal salt of a phosphate ion, monohydrogen phosphate ion or dihydrogen phosphate ion. The chiral amino acid enriched in the D-enantiomer can also be obtained by enzymically converting the corresponding ***hydantoin*** with the aid of a ***hydantoinase*** into the corresponding N-carbamoylamino acid, which is subsequently converted according to the invention into the amino acid enriched in the

D-enantiomer.

L11 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2002 ACS
2002:392371 Document No. 137:108318 Development of Dynamic Kinetic Resolution Processes for Biocatalytic Production of Natural and Nonnatural L-Amino Acids. May, Oliver; Verseck, Stefan; Bommarius, Andreas; Drauz, Karlheinz (Degussa AG, Hanau-Wolfgang, 63457, Germany). Organic Process Research & Development, 6(4), 452-457 (English) 2002. CODEN: OPRDFK. ISSN: 1083-6160. Publisher: American Chemical Society.
AB A review. Two different dynamic kinetic resoln. processes for the prodn. of a no. of natural and nonnatural L-amino acids at 100% chem. and optical yield have recently been established at Degussa. The first process is based on the dynamic kinetic resoln. of 5-monosubstituted ***hydantoins*** using tailor-made whole-cell biocatalysts coexpressing a L- ***carbamoylase*** , a ***hydantoin*** racemase, and a ***hydantoinase*** . The ***hydantoin*** -converting pathway was optimized by adjusting expression levels of the resp. enzymes as well as by inverting the enantioselectivity of the D-selective ***hydantoinase*** . This resulted overall in a 50-fold improved productivity and significant redn. of biocatalyst cost. The second process is based on the dynamic kinetic resoln. of N-acetyl amino acids using an acylase in combination with a novel racemase from Amycolatopsis orientalis subsp. lurida. This racemase could overcome the problem of substrate inhibition and requirement of high concns. of divalent metal ions which limits the use of other N-acylamino acid racemases described in the literature.

L11 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2002 ACS
2002:32038 Document No. 136:182481 ***Hydantoinases*** and related enzymes as biocatalysts for the synthesis of unnatural chiral amino acids. Altenbuchner, Josef; Siemann-Herzberg, Martin; Syldatk, Christoph (Institute of Industrial Genetics, University of Stuttgart, Stuttgart, D-70569, Germany). Current Opinion in Biotechnology, 12(6), 559-563 (English) 2001. CODEN: CUOBE3. ISSN: 0958-1669. Publisher: Elsevier Science Ltd..
AB A review. A cascade of ***hydantoinase*** , N- ***carbamoylase*** and ***hydantoin*** racemase can be used for the prodn. of natural and unnatural chiral D- and L-amino acids from chem. synthesized ***hydantoin*** derivs. Potentially, 100% conversion and 100% optically pure amino acids can be obtained at the same time if racemic substrates are used. Recent research activities conc. on newly isolated or improved enzymes and include directed evolution techniques, structure elucidation, studies of fusion proteins and the use of specially designed whole cell biocatalysts.

L11 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2002 ACS
2002:216 Document No. 136:364581 Cloning and characterization of genes from Agrobacterium sp. IP I-671 involved in ***hydantoin*** degradation. Hils, M.; Muench, P.; Altenbuchner, J.; Syldatk, C.; Mattes, R. (Institute of Industrial Genetics, University of Stuttgart, Stuttgart, 70569, Germany). Applied Microbiology and Biotechnology, 57(5-6), 680-688 (English) 2001. CODEN: AMBIDG. ISSN: 0175-7598. Publisher: Springer-Verlag.
AB Cloning and sequencing of a 7.1 kb DNA fragment from Agrobacterium sp IP I-671 revealed seven open reading frames (ORFs) encoding D- ***hydantoinase*** , D- ***carbamoylase*** and putative ***hydantoin*** racemase, D-amino acid oxidase and NAD(P)H-flavin oxidoreductase. Two incomplete ORFs flanking the ***hydantoin*** utilization genes showed similarities to genes involved in transposition. Expression of the D- ***hydantoinase*** and D- ***carbamoylase*** gene in Escherichia coli gave mainly inactive protein concd. in inclusion bodies, whereas homologous expression on an RSF1010 deriv. increased ***hydantoinase*** and D- ***carbamoylase*** activity 2.5-fold and 10-fold, resp., in this strain. Inactivation of the D- ***carbamoylase*** gene in Agrobacterium sp IP I-671 led to a complete loss of detectable ***carbamoylase*** activity whereas the low ***hydantoinase*** activity remaining after inactivation of the D- ***hydantoinase*** gene indicated the presence of a second ***hydantoinase*** -encoding gene. Two plasmids of 80 kb and 190 kb in size were identified by pulsed-field gel electrophoresis and the cloned ***hydantoin*** utilization genes were found to be localized on the 190

kb plasmid.

L11 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2002 ACS
2001:761352 Document No. 136:289723 Organization of genes responsible for the stereospecific conversion of ***hydantoins*** to .alpha.-amino acids in Arthrobacter aurescens DSM 3747. Wiese, Anja; Syldatk, Christoph; Mattes, Ralf; Altenbuchner, Josef (Institut fur Industrielle Genetik, Universitat Stuttgart, Stuttgart, 70569, Germany). Archives of Microbiology, 176(3), 187-196 (English) 2001. CODEN: AMICCW. ISSN: 0302-8933. Publisher: Springer-Verlag.
AB Arthrobacter aurescens DSM 3747 hydrolyzes stereospecifically 5'-monosubstituted ***hydantoins*** to .alpha.-amino acids. The genes involved in ***hydantoin*** utilization (hyu) were isolated on an 8.7-kb DNA fragment, and by DNA sequence anal. eight ORFs were identified. The hyu gene cluster includes four genes: hyuP encoding a putative transport protein, the ***hydantoin*** racemase gene hyuA, the ***hydantoinase*** gene hyuH, and the ***carbamoylase*** gene hyuC. The four genes are transcribed in the same direction. Upstream of hyuP and in opposite orientation to the hyu genes, three ORFs were found showing similarities to cytochrome P 450 monooxygenase (ORF1, incomplete), to membrane proteins (ORF2), and to ferredoxin (ORF3). ORF8 was found downstream of hyuC and again in opposite orientation to the hyu genes. The gene product of ORF8 displayed similarities to the LacI/GalR family of transcriptional regulators. Reverse transcriptase PCR expts. and Northern blot anal. revealed that the genes hyuPAHC are coexpressed in A. aurescens after induction with 3-N-CH3-IMH. The expression of the hyu operon was not regulated by the putative regulator ORF8 as shown by gene disruption and mobility-shift expts.

L11 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2002 ACS
2001:759219 Document No. 137:184487 Immobilization of the ***hydantoin*** cleaving enzymes from Arthrobacter aurescens DSM 3747. Ragnitz, Kerstin; Pietzsch, Markus; Syldatk, Christoph (Institute of Biochemical Engineering, University of Stuttgart, Stuttgart, D-70569, Germany). Journal of Biotechnology, 92(2), 179-186 (English) 2001. CODEN: JBITD4. ISSN: 0168-1656. Publisher: Elsevier Science Ltd..
AB The immobilization procedure of the two industrially important ***hydantoin*** cleaving enzymes ***hydantoinase*** and L-N-***carbamoylase*** from Arthrobacter aurescens DSM 3747-was optimized. Using different methods (carbodiimide, epoxy activated carriers) it was possible to immobilize the crude ***hydantoinase*** from A. aurescens DSM 3747 to supports contg. primary amino groups with a yield of up to 60%. Immobilization on more hydrophobic supports such as Eupergit C and C 250 L resulted in lower yields of activity, whereas the total protein coupled remained const. All attempts to immobilize the crude L--N-***carbamoylase*** resulted in only low activity yields. Therefore, the enzyme was highly purified and used in immobilization expts. The pure enzyme could easily be obtained in large amts. by cultivation of a recombinant Escherichia coli strain following a three step purifn. protocol consisting of cell disruption, chromatog. on Streamline diethylaminoethyl and Mono Q. The immobilization of the L-N-***carbamoylase*** was optimized with respect to the coupling yield by varying the coupling method as well as the concns. of protein, carrier and carbodiimide. Using 60 mM of water-sol. carbodiimide, nearly 100% of the enzyme activity and protein could be immobilized to EAH Sepharose 4B.

L11 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2002 ACS
2001:247513 Document No. 134:279676 Whole cell catalyst comprising a ***hydantoinase*** , a racemase and a ***carbamoylase*** for the production of amino acids. Altenbuchner, Josef; Mattes, Ralf; Syldatk, Christoph; Wiese, Anja; Wilms, Burkard; Bommarius, Andreas; Tischer, Wilhelm (Degussa-Huels Aktiengesellschaft, Germany; Universitaet Stuttgart; Roche Diagnostics G.m.b.H.). PCT Int. Appl. WO 2001023582 A1 20010405, 51 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO

2000-EP8473 20000831. PRIORITY: US 1999-407062 19990928.
AB A whole cell catalyst is described comprising a ***hydantoinase*** , a racemase and a ***carbamoylase*** . Thus, this catalyst is able to degrade ***hydantoins*** directly into the amino acids. Addnl., a process for the prodn. of this catalysts and for the prodn. of amino acids is claimed. Arthrobacter aurescens DSM 3747 is one of the few isolated microorganisms capable of converting 5-monosubstituted ***hydantoins*** to L-amino acids, but has the disadvantage of low enzyme activity. Thus, the hyuA gene encoding ***hydantoin*** racemase, hyuC gene encoding L-specific ***carbamoylase*** , and the hyuH gene encoding L-specific ***hydantoinase*** were cloned into Escherichia coli under control of the rhamnose-inducible E. coli rhaBAD promoter. Overexpression of these enzymes resulted in efficient conversion of DL-indolylmethylhydantoin into amino acid.

L11 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2002 ACS
2001:167359 Document No. 134:367156 Enzymatic synthesis of enantiomerically enriched D- and L-3-silylated alanines by deracemization of DL-5-silylmethylated ***hydantoins*** . Smith, R. J.; Pietzsch, M.; Waniek, T.; Syldatk, C.; Bienz, S. (Institute of Organic Chemistry, University of Zurich, Zurich, CH-8057, Switz.). Tetrahedron: Asymmetry, 12(1), 157-165 (English) 2001. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 134:367156. Publisher: Elsevier Science Ltd..
AB The ***hydantoinase*** process was shown to be extendable to the prodn. of highly lipophilic, silicon-contg. amino acids. Two ***hydantoinases*** of different origin and stereoselectivities and one L-N- ***carbamoylase*** were used for the highly stereoselective bioconversion of (dimethyl)phenylsilyl- and 1-methyl-1-silacyclopentyl substituted alanine derivs. The enantiomeric purities and abs. configuration of the products were detd. with ref. compds. that were synthesized with the aid of the Evans oxazolidinone auxiliary.

L11 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2002 ACS
2001:129344 Document No. 135:4504 Development of an Escherichia coli whole cell biocatalyst for the production of L-amino acids. Wilms, B.; Wiese, A.; Syldatk, C.; Mattes, R.; Altenbuchner, J. (Institut fur Industrielle Genetik, Universitat Stuttgart, Stuttgart, 70569, Germany). Journal of Biotechnology, 86(1), 19-30 (English) 2001. CODEN: JBITD4. ISSN: 0168-1656. Publisher: Elsevier Science Ltd..
AB A whole cell biocatalyst for the enzymic prodn. of L-amino acids from ***hydantoins*** was created by coexpressing the genes encoding the L-***hydantoinase*** , the L-N- ***carbamoylase*** and the ***hydantoin*** racemase from Arthrobacter aurescens in Escherichia coli. In order to construct a well balanced reaction system the enzymic activity in the cells was varied by using vectors with different copy nos. for expression of the genes. Derivs. of pSC101, pACYC184 and pBR322 were employed for the various constructions and in one construct the ***hydantoinase*** gene was integrated into the E. coli chromosome. All constructs carried the E. coli rhamnose promoter system enabling gene expression control by transcriptional regulation. The productivity for L-tryptophan from the corresponding ***hydantoin*** was more than 6-fold higher than achieved with Arthrobacter aurescens.

L11 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2002 ACS
2000:709239 Document No. 134:29662 Stereoselective synthesis using ***hydantoinases*** and ***carbamoylases*** . Ogawa, Jun; Shimizu, Sakayu (Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Kyoto, Japan). Stereoselective Biocatalysis, 1-21. Editor(s): Patel, Ramesh N. Marcel Dekker, Inc.: New York, N. Y. (English) 2000. CODEN: 69ALWO.
AB A review with 78 refs. A variety of ***hydantoin*** -hydrolyzing enzymes and N-carbamoyl amino acid aminohydrolases are involved in ***hydantoin*** transformations. The combinations of these enzymes provide a variety of processes for the prodn. of optically pure .alpha.-amino acids.

L11 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2002 ACS
2000:707276 Document No. 133:278038 ***Hydantoinase*** variants with improved properties and their use for the production of amino acids. Arnold, Frances H.; May, Oliver; Drauz, Karlheinz; Bommarius, Andreas (California Institute of Technology, USA; Degussa-Huls A.-G.). PCT Int.

Appl. WO 2000058449 A1 20001005, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US8159 20000328. PRIORITY: US 1999-PV126923 19990329; US 1999-PV157427 19991004; US 2000-497585 20000203.

AB ***Hydantoinase*** enzymes which are mutants of Arthrobacter DSM-9771 ***hydantoinase*** are disclosed. The mutants include amino acid substitutions at positions 95, 154, 180, 251 and/or 255 of the wild type ***hydantoinase*** . The mutant ***hydantoinases*** , like the parent ***hydantoinase*** , are used in the prodn. of optically pure amino acids. Thus, a mutant gene encoding Arthrobacter ***hydantoinase*** with I95L, V180A, and Q251R substitutions was prepd. This gene, as well as an Arthrobacter ***carbamoylase*** gene, was expressed in Escherichia coli. When used to prep. L-Met from D,L-Met ***hydantoin*** , the recombinant bacteria produced about 65 mM L-Met per h while the bacteria expressing the wild-type ***hydantoinase*** produced only 8 mM per h. The mutant enzyme was not enantioselective, but was 4-fold more active than the wild-type enzyme.

L11 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2002 ACS

2000:620672 Document No. 133:176261 Process for preparing D-M-amino acids. Kim, Hyung-soon; Hong, Sung-joo; Noh, Bum-sub; Kim, Mook; Choe, Hong-kyu; Park, Young-chol; Cho, Yong-joo (Hanwha Chemical Co., Ltd., S. Korea). Repub. Korea KR 9710133 B1 19970621, No pp. given (Korean). CODEN: KRXXFC. APPLICATION: KR 1994-4847 19940311.

AB Synthetic method of D-M-amino acid using D- ***Hydantoinase*** and D- ***carbamoylase*** is disclosed in this invention. D- ***Hydantoinase*** which hydrates 5-substituted ***Hydantoin*** and D- ***carbamoylase*** which eliminates carbamoyl group from D-N-carbamoyl-M-amino acid are fixed, then put into 5 substituted ***Hydantoin*** soln. or slurry. 5-substituted ***Hydantoin*** is converted into D-M-amino acid and yielded with high purity.

L11 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2002 ACS

2000:569831 Document No. 133:263032 ***Hydantoin*** racemase from Arthrobacter aurescens DSM 3747: heterologous expression, purification and characterization. Wiese, Anja; Pietzsch, Markus; Syldatk, Christoph; Mattes, Ralf; Altenbuchner, Josef (Institut fur Industrielle Genetik, Universitat Stuttgart, Stuttgart, D-70569, Germany). Journal of Biotechnology, 80(3), 217-230 (English) 2000. CODEN: JBITD4. ISSN: 0168-1656. Publisher: Elsevier Science Ltd..

AB In Arthrobacter aurescens DSM 3747 three enzymes are involved in the complete conversion of slowly racemizing 5'-monosubstituted D,L- ***hydantoins*** to L-amino acids, a stereoselective ***hydantoinase*** , a stereospecific L-N- ***carbamoylase*** and a ***hydantoin*** racemase. The gene encoding the ***hydantoin*** racemase, designated hyuA, was identified upstream of the previously described L-N- ***carbamoylase*** gene in the plasmid pAW16 contg. genomic DNA of A. aurescens. The gene hyuA which encodes a polypeptide of 25.1 kDa, was expressed in Escherichia coli and the recombinant protein purified to homogeneity and further characterized. The optimal condition for racemase activity were pH 8.5 and 55.degree. with L-5-benzylhydantoin as substrate. The enzyme was completely inhibited by HgCl2 and iodoacetamide and stimulated by addn. of dithiothreitol. No effect on enzyme activity was seen with EDTA. The enzyme showed preference for ***hydantoins*** with arylalkyl side chains. Kinetic studies revealed substrate inhibition towards the aliph. substrate L-5-methylthioethylhydantoin. Enzymic racemization of D-5-indolylmethylenehydantoin in D2O and NMR anal. showed that the hydrogen at the chiral center of the ***hydantoin*** is exchanged against solvent deuterium during the racemization.

L11 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2002 ACS

2000:541391 Document No. 133:251307 Production of D-Amino Acid Using Whole Cells of Recombinant Escherichia coli with Separately and Coexpressed D- ***Hydantoinase*** and N- ***Carbamoylase*** . Park, Joo-Ho; Kim,

Geun-Joong; Kim, Hak-Sung (Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Taejon, 305-701, S. Korea). Biotechnology Progress, 16(4), 564-570 (English) 2000. CODEN: BIPRET. ISSN: 8756-7938. Publisher: American Chemical Society.

AB A fully enzymic process employing D- ***hydantoinase*** and N- ***carbamoylase*** for the prodn. of D-amino acid from 5'-monosubstituted ***hydantoin*** was developed. For the comparison of the reaction systems using two sequential enzymes, D- ***hydantoinase*** of Bacillus stearothermophilus SD1 and N-carbamoyl-D-amino acidamidohydrolase (N- ***carbamoylase***) of Agrobacterium tumefaciens NRRL B11291 were sep. expressed in each host cell and coexpressed in the same host cell. A high level and constitutive expression of both enzymes in Escherichia coli in a sol. form was achieved using a promoter derived from B. stearothermophilus SD1. The expression levels of both enzymes ranged from 17% to 23% of the total sol. protein, depending on the expression system. In the case of employing sep. expressed enzymes, the product yield of D-hydroxyphenylglycine from D,L-p-hydroxyphenylhydantoin and productivity were 71% and 2.57mM/g-cell/h in 15 h, resp. The accumulation of N-carbamoyl-D-hydroxyphenylglycine was significant over the reaction time. On the other hand, use of coexpressed enzymes resulted in 98% product yield of D-hydroxyphenylglycine in 15 h, minimizing the level of intermediates in the reaction mixt. The productivity of coexpressed whole cell reaction was estd. to be 6.47 mM/g-cell/h in 15 h. The coexpressed system was tested for an elevated concn. of D,L-p-hydroxyphenylhydantoin, and efficient prodn. can be achieved.

L11 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2002 ACS

2000:520535 Document No. 133:252690 Microbial and enzymic synthesis of optically pure D- and L-3-trimethylsilyl-alanine by deracemization of D,L-5-trimethylsilylmethyl- ***hydantoin*** . Pietzsch, Markus; Waniek, Thomas; Smith, Richard J.; Bratovanov, Svetoslav; Bienz, Stefan; Syldatk, Christoph (Institute of Biochemical Engineering, University of Stuttgart, Stuttgart, D-70569, Germany). Monatshefte fuer Chemie, 131(6), 645-653 (English) 2000. CODEN: MOCMB7. ISSN: 0026-9247. Publisher: Springer-Verlag Wien.

AB The stereospecificities of ***hydantoinases*** and N-carbamoyl amino acid amidohydrolases (N- ***carbamoylases***) from different microbial sources were investigated for the stereoselective syntheses of the unnatural silicon-contg. amino acids D- and L-3-trimethylsilyl-alanine (3) from the resp. racemic ***hydantoin*** , D,L-1. In a preparative biotransformation, whole resting cells of Agrobacterium sp. IP I 671, immobilized in a Ca-alginate matrix, were used for the synthesis of amino acid D-3 in 88% yield and 95% enantiomeric excess. Since the purified D-N- ***carbamoylase*** from Agrobacterium sp. IP I 671 was shown to be 100% D-selective, the enantiomeric purity of 95% of D-3 arising from the transformation with the immobilized cells must be explained by the participation of a further, L-selective N- ***carbamoylase*** or, which is more likely, by racemization of the final hydrolysis product by the action of an amino acid racemase. Isolated ***hydantoinases*** from Bacillus thermoglucosidasius, Thermus sp., Arthrobacter aurescens DSM 3745, and Arthrobacter crystallopoietes DSM 20117 turned out to be stereospecific for the conversion of the D-form of ***hydantoin*** D,L-1. The enantiomerically pure L-form of 3 was also prepd. It was synthesized from racemic N-carbamoyl amino acid, D,L-2, by enantiomer-specific hydrolysis of the L-form in presence of L-N- ***carbamoylase*** from Arthrobacter aurescens DSM 3747.

L11 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2002 ACS

2000:327334 Inverting enantioselectivity of a key enzyme creates a viable process for production of L-methionine.. Arnold, Frances H.; Nguyen, Peter T.; May, Oliver (Division of Chemistry and Chemical Engineering, MC 210-41, California Institute of Technology, Pasadena, CA, 91125, USA). Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000, BIOT-112. American Chemical Society: Washington, D. C. (English) 2000. CODEN: 69CLAC.

AB We have dramatically improved the ***hydantoinase*** process for prodn. of L-methionine (L-met) in E. coli by inverting the enantioselectivity of a key enzyme using directed evolution. All known ***hydantoinases*** are selective for D-5-(2-methylthioethyl) ***hydantoin*** (D-MTEH) over the L-enantiomer, which leads to the

accumulation of intermediates and reduced productivity for the L-amino acid. Using random mutagenesis, satn. mutagenesis and screening, we converted the D-selective ***hydantoinase*** from Arthrobacter sp. DSM 9771 (eeD=40% at 30% conversion) into an L-selective enzyme (eeL=20%) and increased its catalytic activity 5-fold. coli cells expressing the evolved L- ***hydantoinase*** , an L-N- ***carbamoylase*** , and a ***hydantoin*** racemase produced 91 mM L-met from 100 mM D,L-MTEH in less than 2 h. The improved ***hydantoinase*** increased productivity 5-fold for > 90% conversion of the substrate. The accumulation of the unwanted intermediate D-carbamoyl-methionine was reduced 4-fold compared to cells with the wild-type pathway. Highly D-selective (<90%eeD at 30% conversion) ***hydantoinase*** mutants were also discovered. Enantioselective enzymes rapidly optimized by directed evolution and introduced into multi-enzyme pathways lead to improved whole-cell catalysts for efficient prodn. of chiral compds.

L11 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2002 ACS

2000:188897 Document No. 132:278227 Inverting enantioselectivity by directed evolution of ***hydantoinase*** for improved production of L-methionine. May, Oliver; Nguyen, Peter T.; Arnold, Frances H. (Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA). Nature Biotechnology, 18(3), 317-320 (English) 2000. CODEN: NABIF9. ISSN: 1087-0156. Publisher: Nature America.

AB Using directed evolution, the ***hydantoinase*** process for prodn. of L-methionine (L-met) in Escherichia coil was improved. This was accomplished by inverting the enantioselectivity and increasing the total activity of a key enzyme in a whole-cell catalyst. The selectivity of all known ***hydantoinases*** for D-5-(2-methylthioethyl) ***hydantoin*** (D-MTEH) over the L-enantiomer leads to the accumulation of intermediates and reduced productivity for the L-amino acid. Random mutagenesis, satn. mutagenesis, and screening were used to convert the D-selective ***hydantoinase*** from Arthrobacter sp. DSM 9771 into an L-selective enzyme and increased its total activity 5-fold. Whole E. coli cells expressing the evolved L- ***hydantoinase*** , an L-N- ***carbamoylase*** , and a ***hydantoin*** racemase produced 91 mM L-met from 100 mM D,L-MTEH in less than 2 h. The improved ***hydantoinase*** increased productivity fivefold for >90% conversion of the substrate. The accumulation of the unwanted intermediate D-carbamoyl-methionine was reduced fourfold compared to cells with the wild-type pathway. Highly D-selective ***hydantoinase*** mutants were also discovered. Enantioselective enzymes rapidly optimized by directed evolution and introduced into multienzyme pathways may lead to improved whole-cell catalysts for efficient prodn. of chiral compds.

L11 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2002 ACS

2000:30890 Document No. 132:218685 Purification of recombinant ***hydantoinase*** and L-N- ***carbamoylase*** from Arthrobacter aurescens expressed in Escherichia coli: comparison of wild-type and genetically modified proteins. Pietzsch, M.; Wiese, A.; Ragnitz, K.; Wilms, B.; Altenbuchner, J.; Mattes, R.; Syldatk, C. (Institute of Biochemical Engineering, University of Stuttgart, Stuttgart, 70569, Germany). Journal of Chromatography, B: Biomedical Sciences and Applications, 737(1 + 2), 179-186 (English) 2000. CODEN: JCBBEP. ISSN: 0378-4347. Publisher: Elsevier Science B.V..

AB Two enzymes, ***hydantoinase*** (HyuH) and L-N- ***carbamoylase*** (HyuC), are required for the biocatalytic prodn. of natural and unnatural, optically pure L-amino acids starting from D,L-substituted ***hydantoins*** using the so called ' ***hydantoinase*** -method'. For the prepn. of immobilized enzymes, which omit several drawbacks of whole cell biocatalysts, purified or at least enriched HyuH and HyuC have to be provided. In order to simplify existing purifn. protocols several genetically modified derivs. of HyuH and HyuC from Arthrobacter aurescens DSM 3747 have been cloned and expressed in E. coli. A fusion protein consisting of maltose-binding protein (MalE) and HyuH resulted in an enhanced soly. of the ***hydantoinase*** , which easily forms inclusion bodies. On the other hand, the fusion protein could easily be purified with high yield (76%) by just one chromatog. step (amylose resin) and the complex purifn. protocol of the wild-type enzyme could therefore be simplified and shortened significantly. Interestingly, the specific activity of the MalE-HyuH fusion protein was as high as the wild-type enzyme despite that the mol. mass was doubled. A second modification of

HyuH carrying a histidine-tag was efficiently bound to a metal affinity matrix but inactivated completely during elution from the column at either low pH or in the presence of imidazole. In the case of HyuC, an aspartate-tag has been added to the biocatalyst to allow an integrated purifn.-immobilization procedure since this enzyme is immobilized efficiently only via its carboxylic groups. The diminished isoelec. point of the Asp-tagged HyuC resulted in a simplified purifn. procedure. Compared to the wild-type enzyme expressed in E. coli HyuC-Asp6 was shifted off the elution range of the contaminating proteins and higher purifn. factors were obtained even in the capturing step. In contrast to HyuH, it was possible to purify a L-N- ***carbamoylase*** carrying a histidine-tag to apparent homogeneity using immobilized metal affinity chromatog. Therefore, the existing three step purifn. protocol was reduced to one chromatog. step and the yield of this relatively unstable protein enhanced remarkably.

L11 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2002 ACS

1999:696975 Document No. 131:350316 One-step production of D-p-hydroxyphenylglycine by recombinant Escherichia coli strains. Chao, Yun-Peng; Fu, Hongyong; Lo, Tsuey-Er; Chen, Po Ting; Wang, Jenn-Jye (Department of Chemical Engineering, Feng Chia University, Taichung, Taiwan). Biotechnology Progress, 15(6), 1039-1045 (English) 1999. CODEN: BIPRET. ISSN: 8756-7938. Publisher: American Chemical Society.

AB The gene encoding D- ***hydantoinase*** from Agrobacterium radiobacter NRRL B11291 was successfully cloned by use of polymerase chain reaction. A pos. clone was scored, and its nucleotide sequence was further analyzed. The anal. by deleting various lengths of nucleotides from the amino terminus of the open reading frame revealed the putative regions for promoter and RBS site. By highly expressing both D- ***hydantoinase*** and ***carbamoylase*** , recombinant Escherichia coli strains were able to convert DL-hydroxyphenyl ***hydantoin*** (DL-HPH) to D-p-hydroxyphenylglycine (D-HPG) with a conversion yield of 97%, accounting for productivity 5 times higher than that obtained by A. radiobacter NRRL B11291. Immobilizing the recombinant cells with .kappa.-carrageenan could also achieve a conversion of 93%, while A. radiobacter NRRL B11291 attained 20% within the same period of reaction time. These results illustrate the feasibility in employing recombinant E. coli to accomplish one-step conversion of DL-HPH to D-HPG. In the process of improving D-HPG prodn., D- ***hydantoinase*** activity was increased 2.57-fold but ***carbamoylase*** activity remained const., which resulted in only a 30% increase in the reaction rate. It suggests that ***carbamoylase*** is the step setting the pace of the reaction. Since the reaction substrate is highly insol., achieving sufficient agitation appears to be an important issue in this heterogeneous system. This view is further supported by the study on repeated use of cells, which shows that to reach a conversion of more than 90% free cells can be recycled six times, whereas immobilized cells can be used only twice. In conclusion, the poor reusability of immobilized cells is due to the fouling on the gel surface.

L11 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2002 ACS

1999:325210 Document No. 131:155052 ***Hydantoinases*** and ***carbamoylases*** of thermophilic bacteria. Sakanyan, Vehary; Weigel, Pierre; Lecocq, Michele; Marc, Frederic; Batisse, Nadine (Unite de Recherche sur la Biocatalyse, Laboratoire de Biotechnologie, Faculte des Sciences et Techniques, Universite de Nantes, Nantes, 44322, Fr.). Recent Research Developments in Microbiology, 2(Pt. 2), 553-565 (English) 1998. CODEN: RDMIFR. Publisher: Research Signpost.

AB A review with 42 refs. on the enzymol. and genetics of thermostable ***hydantoinases*** and ***carbamoylases*** of thermophilic bacteria as potential biocatalysts for large-scale prodn. on proteinogenic and nonproteinogenic amino acids and derivs. Prodn. of optically pure amino acids from racemic ***hydantoins*** is based on two-steps biocatalytic process: (i) the enantioselective ring opening by cyclic amidohydrolases (***hydantoinases***) and (ii) the hydrolysis of the formed N-carbamoyl amino acids by corresponding stereospecific amino acid amidohydrolases (N- ***carbamoylases***). High ***hydantoinase*** and ***carbamoylase*** activities have been detected in strains of Bacillus stearothermophilus, a genus known by its diversity. The ***hydantoinase*** (hyd) and N- ***carbamoylase*** (amaB) genes have been cloned and characterized from several B. stearothermophilus strains.

Similar enzymes appear to exist in some extreme thermophiles as well. The B. stearothermophilus thermostable ***hydantoinase*** was found to be non-stereospecific, however, exhibiting higher D- than L-stereospecificity at the used conditions. Genetic and enzymic data prove that the described ***hydantoinase*** activity is detd. by dihydropyrimidinase, the enzyme of pyrimidine catabolism. The B. stearothermophilus L-***carbamoylase*** and L-aminoacylase are encoded by a bicistronic ama operon. Overexpressed D,L- ***hydantoinase*** and L-N-***carbamoylase*** enabled the resoln. of pure L-amino acids from D,L-***hydantoins*** at high temps. in a reconstituted process.

L11 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2002 ACS

1999:159975 Document No. 130:334514 Immobilization of ***hydantoin*** cleaving enzymes from Arthrobacter aurescens DSM 3747 - effect of the coupling method on the stability of the L-N- ***carbamoylase*** . Pietzsch, M.; Oberreuter, H.; Petrovska, B.; Ragnitz, K.; Syldatk, C. (Institute of Biochemical Engineering, University of Stuttgart, Stuttgart, D-70569, Germany). Progress in Biotechnology, 15(Stability and Stabilization of Biocatalysis), 517-522 (English) 1998. CODEN: PBITE3. ISSN: 0921-0423. Publisher: Elsevier Science B.V..

AB Different coupling methods were tested for the immobilization of the N-carbamoyl-L-amino acid amidohydrolase (L-N- ***carbamoylase***) partially purified from Arthrobacter aurescens DSM 3747. The operational stability of the immobilized biocatalyst was measured using both consecutive batch reactions and continuously operated fixed bed reactors, while the stability of the free L-N- ***carbamoylase*** was investigated using an enzyme membrane reactor. The long term stability of the enzyme was markedly enhanced by all immobilization methods and carriers tested. In consecutive batch reactions the operational stability remained relatively low and significant differences in biocatalysts stability were not obsd. between the different immobilization methods used. In contrast there were significant differences in the stability when the biotransformations were carried out using fixed bed reactors. As a result of this comparison the detn. of the operational stability of the air-sensitive L-N- ***carbamoylase*** on a batch-to-batch basis seems not to be useful.

L11 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2002 ACS

1997:491574 Document No. 127:92191 Thermostable mutants of D-N-.alpha.-***carbamoylase*** with normal catalytic activity for manufacture of D-amino acids from N-carbamoyl amino acids. Grifantini, Renata; Carpani, Giovanna; Galli, Giuliano; Grandi, Guido (Eniricerche S.P.A., Italy). Eur. Pat. Appl. EP 780473 A2 19970625, 19 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1996-118671 19961121. PRIORITY: IT 1995-MI2700 19951221.

AB Amino acid-substituted thermostable mutants of D-N-.alpha.-***carbamoylase*** that have a normal or increased catalytic activity are described for use in the manuf. of D-amino acids for use in sweetener manuf. from carbamoyl amino acids. Specific amino acids of the ***carbamoylase*** of Agrobacterium radiobacter that can be substituted to increase thermostability without adverse effects on catalytic function are identified. The construction of an operon contg. genes for a ***carbamoylase*** and a ***hydantoinase*** is described.

L11 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2002 ACS

1997:453849 Document No. 127:64622 Preparation of D-.alpha.-amino acids, using bacteria transformed with the ***carbamoylase*** - ***hydantoinase*** operon. Grifantini, Renata; Galli, Giuliano; Grandi, Guido; Carpani, Giovanna (Eniricerche S.P.A., Italy). Eur. Pat. Appl. EP 775748 A2 19970528, 16 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1996-117455 19961031. PRIORITY: IT 1995-MI2432 19951123.

AB An improved process is disclosed for the prepn. of D-.alpha.-amino acids by the stereoselective conversion of racemic mixts. of 5-substituted ***hydantoins*** with an enzymic system produced by a microorganism. The improvement consists in the fact that the microorganism used is transformed with the plasmid pSM700 cultivated at a temp. of between 20.degree.C and 28.degree.C. The use of this microorganism allows an improvement in the expression of the enzymic system and an increase in the conversion rate of the racemic ***hydantoin*** to D-.alpha.-amino

acid.

L11 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2002 ACS
1997:278514 Document No. 127:14732 The aim of industrial enzymic amoxycillin production: characterization of a novel ***carbamoylase*** enzyme in the form of a crude, cell-free extract. Louwrier, Ariel; Knowles, Christopher J. (Advanced Biotechnologies Ltd., Epsom, KT19 9QQ, UK). Biotechnology and Applied Biochemistry, 25(2), 143-149 (English) 1997. CODEN: BABIEC. ISSN: 0885-4513. Publisher: Portland Press.
AB Amoxycillin prodn. involves the generation of a racemic mixt. of hydroxyphenylhydantoin by means of the Bucherer synthesis. The ***hydantoin*** is enzymically cleaved by a D-(-)-specific ***hydantoinase*** to form D-(-)-N-carbamoylhydroxyphenylglycine. This is subsequently hydrolyzed by a ***carbamoylase*** enzyme that generates the amino acid deriv., D-(-)-hydroxyphenylglycine. The remaining L-(+)-hydroxyphenylhydantoin spontaneously racemizes, allowing continual cleavage to continue (by the ***hydantoinase*** action) and giving a potential 100% yield of end product from the two-enzyme-catalyzed process, rather than 50%. A novel ***carbamoylase*** from an Agrobacterium species has been studied in a crude (cell-free ext.) form. The temp. stability was shown to be remarkable, with no loss of activity detected after 4 h at 50.degree.C. Kinetic values were calcd. for the enzyme, with a variety of implications for a future industrial process. The substrate specificity, isoelec. point, pH and temp. activity profiles were elucidated, with the aim of generating a com. beneficial method of purifying the enzyme. In addn., the concn.-dependent toxicities of several metal ions were studied; all bivalent ions studied were found to have some detrimental effect on activity.

L11 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2002 ACS
1997:204140 Document No. 126:198637 Production of (R)-tertiary leucine. Bommarius, Andreas; Drauz, Karlheinz; Kottenhahn, Matthias (Degussa Ag, Germany). Ger. Offen. DE 19529211 A1 19970213, 3 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1995-19529211 19950809.
AB A process is claimed in which tert-butylhydantoin is treated with an immobilized (R)-specific ***hydantoinase*** to produce N-carbamoyl-(R)-tert-leucine, which can be transformed ro (R)-tert-leucine using NO2- or (R)- ***carbamoylase*** .

L11 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2002 ACS
1996:251573 Document No. 124:315101 Production of L-methionine from D,L-5-(2-methylthioethyl) ***hydantoin*** by resting cells of a new mutant strain of Arthrobacter species DSM 7330. Wagner, Thomas; Hantke, Britta; Wagner, Fritz (Institute of Biochemistry and Biotechnology, Technical University of Braunschweig, Spielmannstrasse 7, Braunschweig, D-38106, Germany). Journal of Biotechnology, 46(1), 63-8 (English) 1996. CODEN: JBITD4. ISSN: 0168-1656. Publisher: Elsevier.
AB The bioconversion of D,L-5-(2-methylthioethyl) ***hydantoin*** (D,L-MTEH) to the corresponding L-methionine using resting cells of a new isolated mutant strain of Arthrobacter sp. DSM 7330 was studied. In contrast to the parent strain DSM 7330, the resting cells of the new isolated mutant strain DSM 9771 possessed this biocatalytic potency without any need of induction during growth and, on top of this, showed a higher ***hydantoinase*** activity. After further optimizing of the culture medium and with or without the inducer D,L-indolylmethyl-3-methylhydantoin, a 3-fold or 5-fold higher ***hydantoin*** hydrolyzing activity, resp., was obtained compared to the wild-type strain. Using resting cells, the optimal biotransformation parameters were pH 7.5 and 37.degree.C. While the ***hydantoinase*** produced a mixt. of D,L-N-carbamoylmethionine, the L-N- ***carbamoylase*** was proven to be L specific. No inhibition of the enzymic system could be detected up to the max. concn. of soly. of D,L-5-(2-methylthioethyl) ***hydantoin*** (30 g L-1). By a fed-batch technique, up to 120 g L-1 D,L-5-(2-methylthioethyl) ***hydantoin*** could be converted to L-methionine using resting cells of the mutant strain DSM 9771. The yield of this process always reached more than 90%.

L11 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2002 ACS
1995:877657 Document No. 124:56620 Optimal reaction conditions for the enzymic synthesis of optically active D-p-hydroxyphenylglycine from 5-substituted ***hydantoin*** using D- ***hydantoinase*** and N-

. ***carbamoylase*** . Kim, Geun-Joong; Kim, Hak-Sung (Department Biotechnology, Korea Advanced Institute Science and Technology, Taejon, S. Korea). Annals of the New York Academy of Sciences, 750(Enzyme Engineering XII), 185-9 (English) 1995. CODEN: ANYAA9. ISSN: 0077-8923. Publisher: New York Academy of Sciences.

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AB Reaction conditions for the direct enzymic prodn. of D-p-hydroxyphenylglycine for DL-5-substituted ***hydantoin*** I using D- ***hydantoinase*** and N- ***carbamoylase*** from Agrobacterium sp. I-671 are optimized.

L11 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2002 ACS

1995:349517 Document No. 122:234099 Optimization of the enzymic synthesis of D-p-hydroxyphenylglycine from DL-5-substituted ***hydantoin*** using D- ***hydantoinase*** and N- ***carbamoylase*** . Kim, Guen-Joong; Kim, Hak-Sung (Dept. of Biotechnology, Korea Advanced Institute Science and Technology, Taejon, S. Korea). Enzyme and Microbial Technology, 17(1), 63-7 (English) 1995. CODEN: EMTED2. ISSN: 0141-0229. Publisher: Elsevier.

AB D- ***Hydantoinase*** and N- ***carbamoylase*** of Agrobacterium sp. I-671 were partially purified to .apprx.90% purity on SDS-PAGE, and their biochem. properties were characterized. The N- ***carbamoylase*** was severely inhibited by NH4+ coproduced with D-p-hydroxyphenylglycine (D-HPG). For the enhancement of conversion yield, adsorptive removal of NH4+ from the reaction mixt. was attempted, and the conversion yield of D-HPG significantly increased by the addn. of specific adsorbents for NH4+. To det. the optimal ratio of D- ***hydantoinase*** to N- ***carbamoylase*** which minimizes the accumulation of intermediate (N-carbamoyl-D-p-hydroxyphenylglycine) in the direct enzymic prodn. of D-HPG, a sequential reaction was numerically simulated. The simulation results coincided well with exptl. data, and the optimal ratio between D- ***hydantoinase*** and N- ***carbamoylase*** was about 1:3 on a wt. basis.

L11 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2002 ACS

1994:321439 Document No. 120:321439 Adsorptive removal of inhibitory byproduct in the enzymic production of optically active D-p-hydroxyphenylglycine from 5-substituted ***hydantoin*** . Kim, Geun Joong; Kim, Hak Sung (Dep. Biotechnol., Korea Adv. Inst. Sci. Technol., Taejon, S. Korea). Biotechnology Letters, 16(1), 17-22 (English) 1994. CODEN: BILED3. ISSN: 0141-5492.

AB One-step enzymic prodn. of D-p-hydroxyphenylglycine (D-HPG) from 5-substituted ***hydantoin*** was carried out using a bacterium Agrobacterium sp I-671 which possesses D- ***hydantoinase*** and N- ***carbamoylase*** . From the inhibition study, it was found that N- ***carbamoylase*** was severely inhibited by ammonium ions which is coproduced with D-HPG. In order to increase the conversion yield of D-HPG, simultaneous removal of inhibitory byproduct from reaction mixt. was carried out using the specific adsorbents for ammonium ions. The conversion yield of D-HPG reached about 98% in the presence of adsorbents in 27 h, while 50% conversion was obsd. in the absence of adsorbents.

L11 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2002 ACS

1994:186123 Document No. 120:186123 Cloning and expression of gene for D-n-carbamoyl-amino acid amidohydrolase and ***hydantoinase*** of Agrobacterium. Neal, Robert John; Griffin, Alison Michelle; Scott, Miller O'Neill; Shatzman, Allan Richard; Gorham, Hazel Claire (Smithkline Beecham P.L.C., UK; Smithkline Beecham Corp.). PCT Int. Appl. WO 9400577 A1 19940106, 68 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-GB1378 19930630. PRIORITY: GB 1992-13855 19920630; GB 1992-13857 19920630.

AB Processes are provided for the prodn. of ***carbamoylase*** which has the capability of converting D-N-carbamoyl (optionally substituted phenyl) glycine into the corresponding D-(optionally substituted phenyl) glycine by expressing the recombinant DNA encoding the ***carbamoylase*** gene

in a homologous host. Also provided are specific recombinant DNA vectors producing high levels of expression of the ***carbamoylase*** and/or a ***hydantoinase*** in homologous and heterologous hosts and their use in the prodn. of D-.alpha. amino acids.

L11 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2002 ACS
1993:669152 Document No. 119:269152 Continuous microbial conversion of 5-monosubstituted ***hydantoins*** in a cell membrane reactor and product separation via electrodialysis. Noethe, Christian; Millies, Marco; Mewes, Dieter; Syldatk, Christoph; Wagner, Fritz (Univ. Wageningen, Wageningen, 8700 EV, Neth.). Chemie Ingenieur Technik, 65(10), 1224-8 (German) 1993. CODEN: CITEAH. ISSN: 0009-286X.
AB The continuous conversion of D- and L-5-benzylhydantoin to phenylalanine with Arthrobacter aurescens DSM 3747 in a hollow-fiber membrane bioreactor was investigated, together with the feasibility of employing electrodialysis (ED) for product sepn. from unreacted substrates and the intermediate product N-carbamoylphenylalanine. An effective substrate dosing during the initial 30 h ensured that practically complete conversions were obtained. Deactivation of the enzymes involved in the process, L- ***hydantoinase*** and L-N- ***carbamoylase*** , was obsd. after .apprx.30 h, resulting in increased substrate and intermediate product concns. in the reactor outflow. With fresh biomass make-ups or the exchange of the reaction suspension, however, operational times >400 h were attained. Phenylalanine sepn. from the product stream was possible by ED through a C66-5T membrane at pH 2.2.

L11 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2002 ACS
1993:406820 Document No. 119:6820 Characterization of serological properties of polyclonal antibodies produced against enzymes involved in the L-selective cleavage of ***hydantoin*** derivatives. Siemann, Martin; Syldatk, Christoph; Wagner, Fritz (Inst. Biochem. Biotechnol., Tech. Univ. Braunschweig, Braunschweig, 3300, Germany). Biotechnology Letters, 15(1), 1-6 (English) 1993. CODEN: BILED3. ISSN: 0141-5492.
AB Polyclonal antibodies were produced against the highly purified enzymes L- ***hydantoinase*** , ***hydantoin*** -racemase and L-N-carbamoylamino acid amidohydrolase of Arthrobacter aurescens DSM 3747. The serol. properties of these antibodies were characterized. Both the ***hydantoinase*** - and ***carbamoylase*** -antibodies were monofunctional, whereas the ***hydantoin*** -racemase-antibody was addnl. specific against the L- ***hydantoinase*** . Monospecificity was realized after affinity chromatog. Investigations on serol. crossreactions with several linear and cyclic amidases (e.g. ***hydantoinases***) as well as ***hydantoin*** -racemases are demonstrated.

L11 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2002 ACS
1993:192244 Document No. 118:192244 A direct route from ***hydantoins*** to D-amino acids employing a resting cell biocatalyst with D- ***hydantoinase*** and D- ***carbamoylase*** activity. Bommarius, Andreas S.; Kottenhahn, Matthias; Klenk, Herbert; Drauz, Karlheinz (Degussa AG, Hanau, Germany). NATO ASI Series, Series C: Mathematical and Physical Sciences, 381(Microbial Reagents in Organic Synthesis), 161-74 (English) 1992. CODEN: NSCSDW. ISSN: 0258-2023.
AB A report from a symposium on the use of resting Agrobacterium radiobacter cells contg. D- ***hydantoinase*** as well as D- ***carbamoylase*** activity to convert DL- and L- ***hydantoins*** to D-amino acids via carbamoylic acid intermediates. Aided by base catalysis or a racemase, ***hydantoins*** can racemize under the reaction conditions; thus, substrate utilization of to 100% and high yields of D-amino acid products can be achieved.

L11 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2002 ACS
1989:592990 Document No. 111:192990 Production of D- and L-amino acids from D,L-5-monosubstituted ***hydantoins*** . Syldatk, Christoph; Dombach, Giselher; Gross, Christiane; Mueller, Ralf; Wagner, Fritz (Inst. Biochem. Biotechnol., Tech. Univ. Braunschweig, Braunschweig, D-3300, Fed. Rep. Ger.). Annals of the New York Academy of Sciences, 542(Enzyme Eng. 9), 323-9 (English) 1988. CODEN: ANYAA9. ISSN: 0077-8923.
AB The enzymes, D- ***hydantoinase*** and D-N- ***carbamoylase*** , are both strictly stereospecific and, therefore, it is possible to use only the D- ***hydantoinase*** reaction for the prodn. of optically pure

D-amino acids in combination with a second chem. reaction step. In contrast, the stereospecificity of the enzyme, ***hydantoinase*** , involved in the L-specific ***hydantoin*** cleavage is dependent on the substituent in the 5-position of the ***hydantoin*** used as substrate. Only the second reaction catalyzed by the L-N- ***carbamoylase*** is strictly L-specific, so both reactions have to be used in combination for a prodn. of optically pure L-amino acids from D,L-5-monosubstituted ***hydantoins*** . In the L-specific route, neither the racemization nor the poor soly. of the substrate, D,L-5-indolylmethylhydantoin, in water is the rate-limiting step; instead, the second reaction, catalyzed by the enzyme, L-N- ***carbamoylase*** , is the rate-limiting reaction step in this process. Hence, the D- as well as the L-specific cleavage of D,L-5-monosubstituted ***hydantoins*** may have a high potential for industrial employment because both processes have wide substrate specificities and are stereospecific with regard to the prodn. of free amino acids. Resting cells of Arthrobacter crystallopoietes were used as a source of D- ***hydantoinase*** and D-N- ***carbamoylase*** .

L11 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2002 ACS
1987:594833 Document No. 107:194833 Screening method for microorganisms producing L-amino acids from DL-5-monosubstituted ***hydantoins*** . Gross, C.; Syldatk, C.; Wagner, F. (Inst. Biochem. Biotechnol., Tech. Univ. Braunschweig, Braunschweig, D-3300, Fed. Rep. Ger.). Biotechnology Techniques, 1(2), 85-90 (English) 1987. CODEN: BTECE6. ISSN: 0951-208X.
AB The ability of microorganisms to produce ***hydantoinase*** and L-N- ***carbamoylase*** could be established by an overlay assay. Enzyme-producing strains form clear areas around their colonies caused by the cleavage of DL-indolylmethylhydantoin. A second overlayer with a tryptophan-auxotrophic yeast strain enables detection of microorganisms which are able to produce L-tryptophan from DL-indolylmethylhydantoin.

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=> E KRIMMER H/AU
=> S E4
L12          34 "KRIMMER HANS PETER"/AU

=> E MAY O/AU
=> S E3,E10
              9 "MAY O"/AU
             16 "MAY OLIVER"/AU
L13          25 ("MAY O"/AU OR "MAY OLIVER"/AU)

=> E KLEMENT I/AU
=> S E4
L14          17 "KLEMENT INGO"/AU

=> E DRAUZ K/AU
=> S E3-E7
             16 "DRAUZ K"/AU
             10 "DRAUZ KARL HEINZ"/AU
              1 "DRAUZ KARLHEIN"/AU
            221 "DRAUZ KARLHEINZ"/AU
              1 "DRAUZ KARLHEINZ PROF"/AU
L15         249 ("DRAUZ K"/AU OR "DRAUZ KARL HEINZ"/AU OR "DRAUZ KARLHEIN"/AU
                OR "DRAUZ KARLHEINZ"/AU OR "DRAUZ KARLHEINZ PROF"/AU)

=> E REICHERT D/AU
=> S E15
L16          13 "REICHERT DIETMAR"/AU

=> S L12,L13,L14,L15,L16
L17         297 (L12 OR L13 OR L14 OR L15 OR L16)

=> S L17 AND L6
L18          23 L17 AND L6

=> S L18 AND L5
L19          18 L18 AND L5

=> S L19 AND L9
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L20 . 9 L19 AND L9

=> S L17 AND L5
L21 25 L17 AND L5

=> S L21 NOT L10
L22 16 L21 NOT L10

=> D 1-16 CBIB ABS

L22 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS
2002:679201 Hydrolysis and formation of hydantoins. Pietzsch, Markus; Syldatk, Christoph (Institute for Bioprocess Engineering, Department of Microbial Physiology, University of Stuttgart, Stuttgart, 70569, Germany). Enzyme Catalysis in Organic Synthesis (2nd Edition), Volume 2, 761-799. Editor(s): ***Drauz, Karlheinz; Waldmann, Herbert*** . Wiley-VCH Verlag GmbH: Weinheim, Germany. ISBN: 3-527-29949-1 (English) 2002. CODEN: 69DBS5.
AB A review describes the occurrence of the different cyclic amides in nature and their physiol. role in various metabolic pathways. The D- ***hydantoinase*** - and the L-arylalkylhydantoinase processes which are of significance for use in org. synthesis, in particular for the prodn. of natural and non-natural optically pure D- and L-amino acids are also described.

L22 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS
2002:452042 Document No. 137:136892 The Structure of L- ***Hydantoinase*** from Arthrobacter aurescens Leads to an Understanding of Dihydropyrimidinase Substrate and Enantio Specificity. Abendroth, Jan; Niefind, Karsten; ***May, Oliver*** ; Siemann, Martin; Syldatk, Christoph; Schomburg, Dietmar (Institut fuer Biochemie, Universitaet zu Koeln, Cologne, 50674, Germany). Biochemistry, 41(27), 8589-8597 (English) 2002. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.
AB L- ***Hydantoinase*** from Arthrobacter aurescens (L-Hyd) is a member of the dihydropyrimidinases which in turn belong to the cyclic amidases. Dihydropyrimidinases catalyze the reversible hydrolytic ring opening of dihydropyrimidines as the second step in the catabolism of pyrimidines. In biotechnol., their hydrolytic activity on five-membered cyclic diamides (hydantoins) is used in the enantio-specific prodn. of amino acids from racemic hydantoins. L-Hyd differs from most of the other dihydropyrimidinases by an L-enantio specificity and by lacking activity on possible natural substrates such as dihydropyrimidines. In this paper, we describe the three-dimensional structure of L-Hyd which was solved by mol. replacement using a homol. model and subsequently refined to 2.6 .ANG. resoln. Each subunit of the tetrameric L-Hyd consists of an elliptically distorted (.alpha./.beta.)8-barrel domain, which hosts the active site, and a .beta.-sheet domain. In the active site, a binuclear zinc center activates a water mol. for nucleophilic attack on the substrates' amide bond. L-Hyd shows a strong homol. both in fold and in metal coordination in the active site to another dihydropyrimidinase from Thermus sp. (D- ***hydantoinase***) and to a slightly lesser degree to ureases, dihydroorotase and phosphotriesterase. Using the homol. to ureases, a model for the transition state was modeled in the active site of L-Hyd and D- ***hydantoinase*** . This model could provide an explanation for the different substrate and enantio selectivities of both dihydropyrimidinases.

L22 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS
2002:314470 Document No. 136:324174 Use of the acetylamino acid racemase from Amycolatopsis orientalis in the racemization of carbamoylamino acids. Bommarius, Andreas; Verseck, Stefan; ***Drauz, Karlheinz*** ; Kula, Maria-Regina (Degussa Aktiengesellschaft, Germany). Eur. Pat. Appl. EP 1199369 A2 20020424, 8 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR. (German). CODEN: EPXXDW. APPLICATION: EP 2001-123744 20011004. PRIORITY: DE 2000-10050124 20001011.
AB A method is provided for the racemization of N-carbamoylamino acids using the N-carbamoylamino acid racemase of Amycolatopsis orientalis. This method in conjunction with a ***hydantoinase*** and a enantiomer specific carbamoylase can be employed in the prodn. of chiral amino acid

in high yield and high enantiomeric excess.

L22 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS
1999:270336 Document No. 131:55570 Microbial ***hydantoinases*** - industrial enzymes from the origin of life?. Syldatk, C.; ***May, O.*** ; Altnbuchner, J.; Mattes, R.; Siemann, M. (Institute of Biochemical Engineering, University of Stuttgart, Stuttgart, D-70569, Germany). Applied Microbiology and Biotechnology, 51(3), 293-309 (English) 1999. CODEN: AMBIDG. ISSN: 0175-7598. Publisher: Springer-Verlag.
AB A review with approx. 130 refs. ***Hydantoinases*** are valuable enzymes for the prodn. of optically pure D- and L-amino acids. They catalyze the reversible hydrolytic ring cleavage of hydantoin or 5'-monosubstituted hydantoins and are therefore classified in the EC nomenclature as cyclic amidases (EC 3.5.2.). In the EC nomenclature, four different hydantoin-cleaving enzymes are described: dihydropyrimidinase (3.5.2.2), allantoinase (EC 3.5.2.5), carboxymethylhydantoinase (EC 3.5.2.4), and N-methylhydantoinase (EC 3.5.2.14). Beside these, other ***hydantoinases*** with known metabolic functions, such as imidase and carboxyethylhydantoinase and enzymes with unknown metabolic function, are described in the literature and have not yet been classified. An important question is whether the distinct ***hydantoinases*** , which are frequently classified as L-, D-, and non-selective ***hydantoinases*** depending on their substrate specificity and stereoselectivity, are related to each other. In order to investigate the evolutionary relationship, amino acid sequence data can be used for a phylogenetic anal. Although most of these enzymes only share limited sequence homol. (identity < 15%) and therefore are only distantly related, it can be shown (i) that most of them are members of a broad set of amidases with similarities to ureases and build a protein superfamily, whereas ATP-dependent ***hydantoinases*** are not related, (ii) that the urease-related amidases have evolved divergently from a common ancestor and (iii) that they share a metal-binding motif consisting of conserved histidine residues. The difference in enantioselectivity used for the classification of ***hydantoinases*** on the basis of their biotechnol. value does not reflect their evolutionary relationship, which is to a more diverse group of enzymes than was assumed earlier. This protein superfamily probably has its origin in the prebiotic conditions of the primitive earth.

L22 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS
1998:630952 Document No. 129:259349 Biocatalysis to amino acid-based chiral pharmaceuticals - examples and perspectives. Bommarius, Andreas S.; Schwarm, Michael; ***Drauz, Karlheinz*** (Degussa, Hanau, D-63403, Germany). Journal of Molecular Catalysis B: Enzymatic, 5(1-4), 1-11 (English) 1998. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier Science B.V..
AB A review with 12 refs. The search for and development of new pharmaceutically active structures drives the need for new enantiomerically pure compds. (EPC). Many N-contg. structures can be derived beneficially from either L- or D-amino acids. The largest growth occurs in the area of unnatural amino acids. Two examples discussed from the Degussa portfolio concern (i) D-amino acids as components of LHRH antagonists of which the Degussa's Cetrorelix is a prime example as well as (ii) L-tert-leucine, occurring in a fast-growing no. of pharmaceutical compds. under development. For D-amino acids, results of the ***hydantoinase*** /carbamoylase route will be presented while redox catalysis by way of reductive amination is a suitable process to L-tert-leucine. The no. of biocatalytic applications is growing and an updated list is discussed. The presentation will also cover comparisons of biocatalysis with potentially competitive technologies such as enantioselective crystn., chem. asym. synthesis, or chromatog. sepn. of racemates. Future trends relevant to the perspective for biocatalysis include the need for ever more complex chiral mols. as well as shortened development times in the pharmaceutical industry.

L22 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS
1998:533937 Document No. 129:241614 The hydantoin amidohydrolase from Arthrobacter aurescens DSM 3745 is a zinc metalloenzyme. ***May,*** *** Oliver*** ; Siemann, Martin; Siemann, Michael G.; Syldatk, Christoph (Institut fur Bioverfahrenstechnik, Universitat Stuttgart, Stuttgart, D-70569, Germany). Journal of Molecular Catalysis B: Enzymatic, 5(1-4),

367-370 (English) 1998. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier Science B.V..

AB The hydantoin amidohydrolase (***hydantoinase***) from Arthrobacter aurescens DSM 3745 was purified to homogeneity and subjected to metal anal. under at. absorption spectrometry (AAS) and inductive coupled plasma-at. emission spectrometry (ICP-AES). Three independent prepns. of homogeneous enzyme indicated that 1 mol of the active enzyme contains 10 mol zinc ions. This corresponds to 2.5 mol zinc per mol subunit, since the ***hydantoinase*** consists of four identical subunits. Only trace amts. of manganese, magnesia, nickel and cobalt were detected. Other metals were either absent or existed below detection levels.

L22 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS

1998:459932 Document No. 129:256934 Molecular evolution of ***hydantoinases*** . ***May, Oliver*** ; Habenicht, Andreas; Mattes, Ralf; Syldatk, Christoph; Siemann, Martin (Institut Bioverfahrenstechnik, Universitaet Stuttgart, Stuttgart, D-70569, Germany). Biological Chemistry, 379(6), 743-747 (English) 1998. CODEN: BICHF3. ISSN: 1431-6730. Publisher: Walter de Gruyter & Co..

AB The complete amino acid sequence of the ***hydantoinase*** from Arthrobacter aurescens DSM 3745 was derived by automated Edman degrdn. This is the 1st ever reported amino acid sequence of a non-ATP-dependent ***hydantoinase*** , which hydrolyzes 5'-mono-substituted hydantoin derivs. L-selectively. A homol. search performed in protein and nucleic acid databases retrieved only distantly related proteins. All of these are members of the recently described protein superfamily of amidohydrolases related to ureases. Phylogenetic anal. revealed that the novel ***hydantoinase*** forms a new branch sep. from other hydantoin cleaving enzymes like dihydropyrimidinases (EC 3.5.2.2) and allantoinases (EC 3.5.2.5). The authors' results suggests that the enzymes of this protein superfamily have evolved from a common ancestor and therefore are the product of divergent evolution. The authors show further that the enclosed gene families developed very early in evolution, probably prior to the formation of the 3 domains, Archaea, Eukarya and Bacteria. ***Hydantoinases*** related to ATP-dependent N-ethylhydantoinases (EC 3.5.2.14) or 5-oxoprolinases (EC 3.5.2.9) do not belong to this superfamily.

L22 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS

1998:403927 Document No. 129:146135 Substrate-dependent enantioselectivity of a novel ***hydantoinase*** from Arthrobacter aurescens DSM 3745: Purification and characterization as new member of cyclic amidases. ***May, Oliver*** ; Siemann, Martin; Pietzsch, Markus; Kiess, Michael; Mttes, Ralf; Syldatk, Christoph (Inst. Bioverfahrenstechnik, Univ. Stuttgart, Stuttgart, 70569, Germany). Journal of Biotechnology, 61(1), 1-13 (English) 1998. CODEN: JBITD4. ISSN: 0168-1656. Publisher: Elsevier Science B.V..

AB A ***hydantoinase*** from Arthrobacter aurescens DSM 3745 has been purified to homogeneity with a yield of 77% using a three-step purifn. procedure. The active enzyme is a tetramer consisting of four identical subunits, each with a mol. mass of 49670 Da as detd. by mass spectrometry. The N-terminal amino acid sequence of the enzyme indicates sequence identities to cyclic amidases involved in the nucleotide metab. as the D- ***hydantoinase*** from Agrobacterium radiobacter (53%), the D-selective dihydropyrimidinase from Bacillus stearothermophilus (38%), the allantoinase from Rana catesbeiana (26%), as well as to the catalytic subunit of the urease from Heliobacter pylori (50%). However, all studies based on substrate-dependent growth, induction and catalytic behavior documented the novelty of the bacterial ***hydantoinase*** and that its physiol. role is not related to any of these enzymes or known metabolic pathways. Its substrate specificity differs from ***hydantoinases*** listed in Enzyme Nomenclature and is rather more predominant for the cleavage of aryl- than for alkyl-hydantoin derivs. It is shown that the stearoselectivity of this enzyme depends on the substrate used for bioconversion: although it is strictly L-selective for the cleavage of D,L-5-indolylmethylhydantoin, it appears to be D-selective for the hydrolysis of D,L-methylthioethylhydantoin. Due to these findings we conclude that this novel bacterial ***hydantoinase*** should be classified as a new member of the EC-group 3.5.2 of cyclic amidases.

L22 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2002 ACS

1998:380760 Document No. 129:133018 Catalytic and structural function of zinc for the ***hydantoinase*** from Arthrobacter aurescens DSM 3745. ***May, Oliver*** ; Siemann, Martin; Siemann, Michael Georg; Syldatk, Christoph (Institut fur Bioverfahrenstechnik, Universitat Stuttgart, Stuttgart, D-70569, Germany). Journal of Molecular Catalysis B: Enzymatic, 4(4), 211-218 (English) 1998. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier Science B.V..

AB The metal dependency of hydantoin amidohydrolase/ ***hydantoinase*** (I) from A. aurescens DSM 3745 was analyzed based on kinetic studies of metal/chelator-caused enzyme inactivation, denaturation and reactivation, accompanied by the identification of specific metal binding ligands. I could be inactivated by metal-chelating agents and, apart from the loss of its activity, completely dissocd. into its subunits. Enzyme activity could be restored from recollected monomers by the addn. of Co^{2+}, Mn^{2+}, or Zn^{2+}, whereas Ni^{2+} and Mg^{2+} remained ineffective. Subjection of I to metal anal. revealed a content of 10 mol Zn/mol I. Zn played an essential role not only for the catalytic activity but also for the stabilization of the active quaternary structure of the I. Histidine-specific chem. modification of I caused complete loss of catalytic activity and revealed His residues as putative Zn-binding ligands. Both, the metal/chelator-caused enzyme inactivation as well as the metal-caused enzyme reactivation, could be reduced in the presence of the substrate. Therefore, it is very likely that at least 1 metal cation acts specifically near or at the active site of the enzyme.

L22 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS

1998:274112 Document No. 129:51176 A new method for the detection of ***hydantoinases*** with respect to their enantioselectivity on acrylamide gels based on enzyme activity stain. ***May, Oliver*** ; Siemann, Martin; Syldatk, Christoph (Institut fur Bioverfahrenstechnik, Universitat Stuttgart, Stuttgart, D-70569, Germany). Biotechnology Techniques, 12(4), 309-312 (English) 1998. CODEN: BTECE6. ISSN: 0951-208X. Publisher: Chapman & Hall.

AB A new and highly sensitive method was developed for the identification of ***hydantoinases*** on acrylamide gels. For this purpose, cell-lysates from different natural isolates are subjected on PAGE under non-denaturating conditions. The resp. localization of the ***hydantoinase*** is obtained by in situ product pptn. during the reverse enzyme reaction: in contrast to the used substrate (N-carbamoyltryptophan), the product (indolylmethylhydantoin) is barely sol. and gives a dense pptn. dot caused by crystn. of the product inside of the polyacrylamide gel at the position corresponding to the location of the enzyme. This method can also be used for the subsequent differentiation between L- and D-selective ***hydantoinases*** , since L- or D-carbamoyltryptophan is used as substrate.

L22 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS

1997:461254 Document No. 127:162073 Chiral amino acids. A versatile tool in the synthesis of pharmaceuticals and fine chemicals. ***Drauz,*** *** Karlheinz*** (Specialty Chemicals Division, Degussa A.-G., Hanau, D-63403, Germany). Chimia, 51(6), 310-314 (English) 1997. CODEN: CHIMAD. ISSN: 0009-4293. Publisher: Neue Schweizerische Chemische Gesellschaft.

AB A brief review with 7 refs. Methods of prepg. enantiomerically pure amino acids esp. focusing on amino-acylase-based resoln. of D,L-acetyl amino-acid precursors, synthesis of D-amino acids using a ***hydantoinase*** system, and the cofactor-dependent enzymic reductive amination of .alpha.-keto acids to L-amino acids are described. Examples are given for bulk actives, based on L- and D-amino acids and peptides. L- And D-Tle (L-/D-2-amino-3,3-dimethylbutanoate) are important mols. for synthesizing drugs and a great variety of chiral auxiliaries. A new chromatog. sepn. of bulky-side-chain amino acids in a preparative scale is described, giving both enantiomers in >99% ee.

L22 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS

1996:734696 Document No. 126:16235 Crystallization and preliminary x-ray analysis of a ***hydantoinase*** from Arthrobacter aurescens DSM 3745. ***May, O.*** ; Siemann, M.; Syldatk, C.; Niefind, K.; Schomburg, D. (Inst. Bioverfahrenstechnik, Univ. Stuttgart, Stuttgart, 70569, Germany). Acta Crystallographica, Section D: Biological Crystallography, D52(6), 1209-1210 (English) 1996. CODEN: ABCRE6. ISSN: 0907-4449. Publisher: Munksgaard.

AB L- ***Hydantoinase*** from A. aurescens DSM 3745 was purified to homogeneity and crystd. from polyethylene glycol solns. in a form suitable for x-ray diffraction anal. The crystals were grown by the sitting-drop variant of the vapor-diffusion method. The x-ray diffraction studies showed that the crystals belong to monoclinic space group P21 with a = 111.2, b = 74.4, c = 146.5 .ANG., and .beta. = 106.7.degree.. The asym. unit contained 4 monomers related by 222 symmetry. The crystals diffracted to at least 2.6 .ANG..

L22 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS
1995:506335 Document No. 122:237925 Production of cyclic N-carbamoyl-D-amino acids. Bommarius, Andreas; Schaefer, Matthias; ***Drauz, Karlheinz*** (Degussa A.-G., Germany). Ger. Offen. DE 4330678 A1 19950316, 4 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1993-4330678 19930910.
AB A process for the prodn. of cyclic N-carbamoyl-D-amino acids from the corresponding hydantoins with the use of a ***hydantoinase*** is disclosed.

L22 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2002 ACS
1995:319864 Document No. 122:104046 Microorganisms, their use and method of production of L-.alpha.-amino acids. Wagner, Fritz; Voelkel, Dirk; Bommarius, Andreas; ***Drauz, Karlheinz*** (Degussa A.-G., Germany). Eur. Pat. Appl. EP 625571 A2 19941123, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE. (German). CODEN: EPXXDW. APPLICATION: EP 1994-107323 19940511. PRIORITY: DE 1993-4316928 19930519.
AB N-5-Monosubstituted D-, L-, or DL-hydantoins or their corresponding carbamoyl-.alpha.-amino acids are converted to L-amino acids in high yields by Arthrobacter DSM 7329 and DSM 7330.

L22 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS
1993:579206 Document No. 119:179206 Membrane bioreactors for the production of enantiomerically pure .alpha.-aminoacids. Bommarius, A. S.; ***Drauz, K.*** ; Groeger, U.; Wandrey, C. (Degussa AG, Hanau, Germany). Chirality Ind., 371-97. Editor(s): Collins, Andrew N.; Sheldrake, G. N.; Crosby, J. Wiley: Chichester, UK. (English) 1992. CODEN: 59DGAP.
AB A review with 51 refs. This chapter describes some of the methods for large-scale prodn. of enantiomerically pure .alpha.-amino acids and the role of membrane reactors within these processes. Following the discussion of the acylase, amidase and ***hydantoinase*** processes some novel developments with enzymes to be used in membrane bioreactors are presented: utilization of racemases, prodn. of L-ornithine with arginase and L-proline with proline acylase, the C-terminal deamidation of peptides with peptide amidase and novel processes for enzymic peptide synthesis.

L22 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2002 ACS
1988:185294 Document No. 108:185294 Manufacture of optically active amino acids by microbial or enzymic resolution of racemic amino acid carbamates. Sambale, Clemens; Kula, Maria Regina; Hummel, Werner; ***Drauz,*** *** Karlheinz*** (Gesellschaft fuer Biotechnologische Forschung m.b.H., Fed. Rep. Ger.). Ger. Offen. DE 3606401 A1 19870903, 9 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1986-3606401 19860227.
AB Optically active amino acids (or norephedrine) are prepd. by stereoselective hydrolysis of racemic carbamates or oxycarbonyl derivs. by microbes or enzymes. Microorganisms were isolated from carbamate pesticide-treated land and selected for their ability to hydrolyze N-(methoxycarbonyl)-DL-valine (I), etc. One of the isolated strains converted 92.86% of I to L-valine. Other com. available enzymes (carboxylesterase from pig liver; ***hydantoinase*** from Pseudomonas fluorescens; urease; acetylcholinesterase from eel, or bovine or human erythrocytes; and acylase from yeast or pig kidney) were tested for their utility in this process. Only the latter 4 were effective.

	L #	Hits	Search Text	DBs
1	L1	92	HYDANTOINASE	USPAT ; US-PG PUB
2	L2	22	CARBAMOYLASE	USPAT ; US-PG PUB
3	L3	7069	HYDANTOIN	USPAT ; US-PG PUB
4	L4	50	ALLYSINE	USPAT ; US-PG PUB
5	L5	1	L1 AND L2 AND L3 AND L4	USPAT ; US-PG PUB
6	L6	19	L1 AND L2	USPAT ; US-PG PUB
7	L7	18	L6 NOT L5	USPAT ; US-PG PUB

```
FILE 'REGISTRY' ENTERED AT 09:42:11 ON 22 NOV 2002

=> S HYDANTOINASE/CN
L1             1 HYDANTOINASE/CN

=> S HYDANTOIN/CN
L2             1 HYDANTOIN/CN

=> S ALLYSINE/CN
L3             1 ALLYSINE/CN

FILE 'CAPLUS' ENTERED AT 09:43:13 ON 22 NOV 2002

=> S HYDANTOINASE OR L1;S HYDANTOIN OR L2;S ALLYSINE OR L3
             274 HYDANTOINASE
              41 HYDANTOINASES
             279 HYDANTOINASE
                   (HYDANTOINASE OR HYDANTOINASES)
             334 L1
L4           389 HYDANTOINASE OR L1


            6333 HYDANTOIN
            2073 HYDANTOINS
            6981 HYDANTOIN
                   (HYDANTOIN OR HYDANTOINS)
            1217 L2
L5          7192 HYDANTOIN OR L2


              70 ALLYSINE
               1 ALLYSINES
              70 ALLYSINE
                   (ALLYSINE OR ALLYSINES)
              62 L3
L6           112 ALLYSINE OR L3

=> S L6 AND L4
L7             1 L6 AND L4

=> S L5 AND L6
L8             4 L5 AND L6

=> S L7,L8
L9             4 (L7 OR L8)

=> D 1-4 CBIB ABS

L9   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
2002:107576   Document No. 136:149991  Process for the preparation of
       ***allysine***   acetal.  Krimmer, Hans-Peter; May, Oliver; Klement, Ingo;
     Drauz, Karlheinz; Reichert, Dietmar (Degussa A.-G., Germany).  PCT Int.
     Appl. WO 2002010424 A1 20020207, 16 pp.  DESIGNATED STATES: W:  AU, BR,
     CA, CN, CZ, HR, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RU, SG, SI, SK,
     ZA; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
     PT, SE, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO 2001-EP7387
     20010628.  PRIORITY: DE 2000-10037115 20000728.
GI


/ Structure 1 in file .gra /


AB   The present invention relates to the prepn. of compds. of formula (I) from
     the corresponding   ***hydantoins***   (II) by means of an enzymic process
     where R represents C1-C8 alkyl, C2-C4 alkenyl, preferably ethylenyl,
     C6-C18 aryl, C7-C19 aralkyl, or C1-C8 acyl.  The   ***hydantoin***   , II
     is subjected to a reaction catalyzed   ***hydantoinase***   ,
       ***hydantoin***   racemase and a L- or D- specific carbamoylase.  The
     L-compd. is preferably formed.
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L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
2001:435820 Document No. 135:121212 Enzymatic synthesis of chiral intermediates for Omapatrilat, an antihypertensive drug. Patel, Ramesh N. (Enzyme Technology, Process Research & Development, Bristol-Myers Squibb Pharmaceutical Research Institute, New Brunswick, NJ, 08903, USA). Biomolecular Engineering, 17(6), 167-182 (English) 2001. CODEN: BIENFV. ISSN: 1389-0344. Publisher: Elsevier Science B.V..

AB A review with 50 refs. Biocatalytic processes were used to prep. chiral intermediates required for the synthesis of Omapatrilat 1 by three different routes. The synthesis and enzymic conversion of 2-keto-6-hydroxyhexanoic acid 3 to L-6-hydroxynorleucine 2 was demonstrated by reductive amination using beef liver glutamate dehydrogenase. To avoid the lengthy chem. synthesis of the ketoacid 3, a second route was developed to prep. the ketoacid by treatment of racemic 6-hydroxy norleucine [readily available from hydrolysis of 5-(4-hydroxybutyl) ***hydantoin*** 4] with D-amino acid oxidase from porcine kidney or Trigonopsis variabilis followed by reductive amination to convert the mixt. completely to L-6-hydroxynorleucine in 98% yield and 99% enantiomeric excess (e.e.). The enzymic synthesis of (S)-2-amino-5-(1,3-dioxolan-2-yl)-pentanoic acid (***allysine*** ethylene acetal, 5) was demonstrated using phenylalanine dehydrogenase (PDH) from T. intermedius. Phenylalanine dehydrogenase was cloned and overexpressed in Escherichia coli and Pichia pastoris. Using PDH from E. coli or P. pastoris, the enzymic process was scale-up to prep. kg quantity of ***allysine*** ethylene acetal 5. The reaction yields of > 94% and e.e. of > 98% were obtained for ***allysine*** ethylene acetal 5. An enzymic process was developed for the synthesis of [4S-(4a, 7a, 10ab)]1-octahydro-5-oxo-4 [[(phenylmethoxy)carbonyl]amino]-7H-pyrido-[2,1-b] [1,3]thiazepine-7-carboxylic acid [BMS-199541-01]. The enzymic oxidn. of the .epsilon.-amino group of lysine in the dipeptide dimer N2-(N[[(phenyl-methoxy)carbonyl] L-homocysteinyl] L-lysine)-1,1-disulfide [BMS-201391-01] to produce BMS-199541-01 using a novel L-lysine .epsilon.-aminotransferase (LAT) from Sphingomonas paucimobilis SC 16113 was demonstrated. This enzyme was overexpressed in E. coli and a process was developed using the recombinant enzyme.

L9 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
1989:478570 Document No. 111:78570 ***Allysine*** peptides and derivatives. Doelz, R.; Heidemann, E. (Dep. Protein Leather, Inst. Macromol. Chem., Darmstadt, Fed. Rep. Ger.). International Journal of Peptide & Protein Research, 32(4), 307-20 (English) 1988. CODEN: IJPPC3. ISSN: 0367-8377. OTHER SOURCES: CASREACT 111:78570.

AB ***Allysine*** , OCH(CH2)3CH(NH2)CO2H, which is synthesized enzymically in vivo starting from lysine, is a very important crosslink precursor in proteins. The chem. synthesis of ***allysine*** derivs. starting from 3,4-dihydro-2H-pyran is described. Two independent synthetic routes for the prepn. of ***allysine*** peptides and derivs. are presented. The synthesized compds. are characterized by spectroscopic methods including 13C NMR. The reactivity of the aldehyde function is shown to be extremely high. An unexpected nucleophilic attack of the ***allysine*** amide nitrogen at the aldehyde group is described. This ring closure reaction is not expected to occur in native collagen; however, denatured peptides contg. ***allysine*** may react similarly to the model peptides.

L9 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
1989:419605 Document No. 111:19605 Reactivity of the ***allysine*** aldehyde group. Doelz, R.; Heidemann, E. (Dep. Protein Leather, Inst. Macromol. Chem., Darmstadt, FRG-6100, Fed. Rep. Ger.). Connective Tissue Research, 18(4), 255-68 (English) 1989. CODEN: CVTRBC. ISSN: 0300-8207.

AB ***Allysine*** is a very important crosslink precursor in connective tissue proteins. The reactions of phthalylallysine p-nitrobenzyl ester (I) which is a suitable compd. for investigationg the reactions of the aldehyde group in vitro were described. Crosslinked compds. were synthesized by mixing suitable stoichiometric amts. of I and nucleophiles in aq. org. solvents. The results were compared with the reaction pathways which have been proposed for crosslink synthesis in vivo.

=> S CARBAMOYLASE
82 CARBAMOYLASE
10 CARBAMOYLASES
L10 85 CARBAMOYLASE

(CARBAMOYLASE OR CARBAMOYLASES)

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=> S L10 AND L6
L11           1 L10 AND L6

=> S L11 NOT L9
L12           0 L11 NOT L9
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DERWENT-ACC-NO: 1999-486364
DERWENT-WEEK: 199941

TITLE: New process for preparation of optically active alpha-aminoadipic acid-gamma-semialdehyde ethylene acetal - useful for production of medicines and cosmetics

PATENT-ASSIGNEE: DAIICHI KAKAGU YAKUHIN KK[DAIIN]

PRIORITY-DATA: 1998JP-0016842 (January 29, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 11206397 A	August 3, 1999	N/A	006	C12P 017/04

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-DATE
JP11206397A	N/A	1998JP-0016842	January 29, 1998

INT-CL (IPC): C07D317/30; C07M007:00 ; C12P017/04 ; C12P017/04 ; C12R001:06

ABSTRACTED-PUB-NO: JP11206397A
BASIC-ABSTRACT: A process for preparation of the optically active compound and its salt shown by formula (2-3) by treatment of compound(s) shown by formulae (1-1) and/or (2-2) with cells of Arthrobacter microorganisms or their treated cells is new.

USE - Compound (3) is a useful intermediate of medicines and cosmetics.

CHOSEN-DRAWING: Dwg.0/0

TITLE-TERMS:
NEW PROCESS PREPARATION OPTICAL ACTIVE ALPHA ACID GAMMA ETHYLENE ACETAL USEFUL
PRODUCE MEDICINE COSMETIC

DERWENT-CLASS: B03 D16 D21 E13

CPI-CODES: B04-F10A; D05-H04; D05-H08; E07-A04;

CHEMICAL-CODES:
Chemical Indexing M2 *01*
Fragmentation Code
F012 F140 H1 H100 H181 J0 J011 J1 J171 M280

M314 M321 M332 M343 M349 M371 M391 M413 M510 M521
M530 M540 M720 M903 M904 N131 N205 N209 N231 N341
N361
Markush Compounds
199941-FDE01-K 199941-FDE01-P

Chemical Indexing M3 *01*
Fragmentation Code
F012 F140 H1 H100 H181 J0 J011 J1 J171 M280
M314 M321 M332 M343 M349 M371 M391 M413 M510 M521
M530 M540 M720 M903 M904 N131 N205 N209 N231 N341
N361
Markush Compounds
199941-FDE01-K 199941-FDE01-P

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1999-142710

CLIPPEDIMAGE= JP411206397A

PAT-NO: JP411206397A

DOCUMENT-IDENTIFIER: JP 11206397 A

TITLE: PRODUCTION OF OPTICALLY ACTIVE ALPHA-AMINOADIPIC ACID-GAMMA-SEMIALDEHYDE ETHYLENE ACETAL

PUBN-DATE: August 3, 1999

INVENTOR-INFORMATION:

NAME	COUNTRY
TAKIMOTO, YUKIYA	N/A
SHITO, TOSHIAKI	N/A
MASUMI, FUMIO	N/A

ASSIGNEE-INFORMATION:

NAME	COUNTRY
DAI ICHI PURE CHEM CO LTD	N/A

APPL-NO: JP10016842

APPL-DATE: January 29, 1998

INT-CL (IPC): C12P017/04;C07D317/30

ABSTRACT:

PROBLEM TO BE SOLVED: To industrially and advantageously produce the subject compound useful as an intermediate, etc., for medicines and cosmetics by making microorganisms of the genus Arthrobacter act on a specific compound derived from glutaraldehyde monoethylene acetal.

SOLUTION: A microorganism belonging to the genus Arthrobacter [e.g. Arthrobacter sp. DP-B-1001 (FERM P-8190)] or its microbial cell or a treated microbial cell is made to act on a compound obtained by reacting glutaraldehyde monoethylene acetal with hydrogen cyanide (salt), ammonia (salt) and gaseous carbon dioxide, a (hydrogen)carbonic salt or a carbamic salt, etc., in an aqueous solvent and represented by formulae I and/or II to thereby industrially and advantageously produce the objective optically active